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| 07/827,906      | 01/30/1992  | KENNETH A. BARTON    | 28079/41333         | 3375             |

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| EXAMINER |
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KUBELIK, ANNE R

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1638

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02/25/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 07/827,906             | BARTON ET AL.       |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Anne R. Kubelik        | 1638                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 27-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 27-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/8/09, 1/21/09, 2/10/09</u> .                                | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Claims 27-44 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The objection to claims 23-27 because of informalities is obviated by Applicant's cancellation or amendment of the claims.
4. The objection to claims 24 and 26 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is obviated by Applicant's cancellation of the claims.
5. The rejection of claims 23-32 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in light of Applicant's cancellation or amendment of the claims.
6. The rejection of claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's cancellation of the claims.
7. The rejection of claims 27 and 30-32 are rejected under 35 U.S.C. 102(g) as being anticipated by Fischhoff et al (2003/0192078, which is a division of application 08/434,105) is withdrawn in light of Applicant's amendment of the claims.

***Claim Rejections - 35 USC § 112***

8. Claims 27-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 18 June 2008, as applied to claims 23-32. Applicant's arguments filed 18 November 2008 have been fully considered but they are not persuasive.

Neither the instant specification nor the originally filed claims appear to provide support for modifying the codons for at least the first 25 amino acids in any coding sequence as in claims 28, 33 and 40. The specification only provides support for modifying "about 25 codons" at the N' terminal end of the Bt sequence used in the Examples (pg 13, lines 15-22).

Neither the instant specification nor the originally filed claims appear to provide support for substituting at least 59 amino acids in any coding sequence as in claim 29. The specification only provides support for modifying 59-138 codons of the Bt sequence used in the Examples (pg 13, line 9).

Applicant urges that the application teaches that expression enhancement is principally due to substitutions at the amino terminus, with mention of 25, 59 and 138 codons (response pg 11-12).

This is not found persuasive because this mention in the specification specially refers to the examples, not to any coding sequence.

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Applicant urges that the discussion is about the lessons learned from the examples (response pg 12).

This is not found persuasive because these particular numbers are mentioned only in context of the examples, not in a context that says that substitutions of the first 25, 59 or 138 codons could be applied to any coding sequence. See pg 13, lines 7-16

In the following example, the coding region of the protein expression cassette was altered by as few as 59 to as many as 138 codons, all at the amino terminal end of the protein or the 5' end of the coding region. Since the results did not seem to vary greatly based on the length of the substituted codons, it is possible that the increased expressional efficiency is due principally to the substitutions at the amino-terminal, or 5', end of the coding sequence, perhaps those in the first 25 codons.

Further, there is no support for substituting the codons for at least 59 or at least the first 25 amino acids.

Neither the instant specification nor the originally filed claims appear to provide support for substituting merely at the 5' end of any coding sequence as in claim 39. The specification only provides support for modifying codons at the 5' end of the Bt sequence used in the Examples (paragraph spanning pg 9-10).

Thus, such claims constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the claims or to cancel the new matter.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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10. Claims 27-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischhoff et al (2003/0192078, which is a division of application 08/434,105).

The claims are drawn to a method of modifying a coding sequence by substituting codons used at the highest frequency in the instant Table 1.

On 12 December 1986 (see interference decision in the instant case mailed 29 January 2004), Fischhoff et al reduced to practice a method of designing a synthetic *Bacillus thuringiensis* endotoxin gene, said method comprising modifying the native sequence by substituting at least some of the codons in the native coding sequence with codons for the same amino acids but that have the highest frequency in plant genes, such as their Table I (¶54-56). Fischhoff et al also disclose attaching a promoter to the modified sequence (¶57-63).

Fischhoff et al do not teach the instant codon usage table.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of modifying codon usage in a gene to match that of the plant genome as taught by Fischhoff et al to use the codons that have the highest frequency in the instant table I. One of ordinary skill in the art would have been motivated to do so because which codons are determined to be at the highest frequency is determined by the genes used to make the codon usage table. The number of possible codons for each amino acid is limited; thus, there are a limited number of possible codon tables showing codons that have the highest frequency. Unless one such table provides unexpected results, each table is obvious over all the others. Substituting all the codons for those used at the highest frequency would be substituting at least the first 25 or at least 59 codons at the 5' end or codons at the 5' end.

***Double Patenting***

11. Claims 27, 30-32, 38 and 41-44 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,833,449. The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 June 2008, as applied to claims 23-32. Applicant's arguments filed 18 November 2008 have been fully considered but they are not persuasive.

Although the conflicting claims are not identical, they are not patentably distinct from each other. A synthetic nucleic acid encoding a particular Cry endotoxin, wherein at least a portion of the coding sequence for the endotoxin exclusively uses the codons in the instant Fig 1 used at the highest frequency, as claimed in the issued patent, makes obvious a method of making a coding sequence for a Bt endotoxin using the codons in the instant Fig 1 used at the highest frequency, as claimed in the instant application. As the method steps are the same, methods of increasing the level of efficiency in expression of a Bt insecticidal protein are also made obvious. It would be obvious to one of skill in the art to attach regulatory sequences to the coding sequence, as expression in a plant requires plant regulatory sequences. Substituting all the codons for those used at the highest frequency would be substituting at least the first 25 or at least 59 codons at the 5' end or codons at the 5' end.

Applicant urges that a nucleic acid is a product, not a method, and a nucleic acid does not teach or suggest the method by which it is made (response pg 15-16).

This is not found persuasive because claims 1-3 of '449 refers to making the sequence by selecting from the codons in Fig 1 used at the highest frequency. Nucleic acids that are claimed as a product-by-process make the process obvious.

Applicant urges that although both sets of claims refer to the codons in Figure 1, this observation is about what is disclosed by the claims, rather than what is defined by the claims; it is not proper to analyze claims for observation they suggest. The Office has not said why the product makes obvious the method of making it (response pg 16).

This is not found persuasive because a product in which each codon is the codons in Fig 1 used at the highest frequency process makes obvious of method of making the product by modifying the coding sequence by substituting the native codons for the codons in Fig 1 used at the highest frequency.

Applicant urges that a two-way test must be used because of the prosecution delay cause by the interference (response pg 16).

This is not found persuasive because two conditions must be met for the two-way test must be used; in addition to administrative delay, Applicant must show that they could not have filed the claims in a single application (See MPEP 804 IIB1b). Applicant has not shown that they could not have filed the claims in a single application. Thus, the one-way test applies.

### ***Conclusion***

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is



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February 25, 2009

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638